



UNIVERSITÀ
DEGLI STUDI
FIRENZE

FLORE

Repository istituzionale dell'Università degli Studi di Firenze

Glycated hemoglobin in ST-elevation myocardial infarction without previously known diabetes: Its short and long term prognostic role

Questa è la Versione finale referata (Post print/Accepted manuscript) della seguente pubblicazione:

Original Citation:

Glycated hemoglobin in ST-elevation myocardial infarction without previously known diabetes: Its short and long term prognostic role / C.Lazzeri; S.Valente; M.Chiostrì; C.Picariello; P.Attanà; G.F.Gensini. - In: DIABETES RESEARCH AND CLINICAL PRACTICE. - ISSN 0168-8227. - ELETTRONICO. - 95(2012), pp. 14-16.

Availability:

This version is available at: 2158/592662 since:

Terms of use:

Open Access

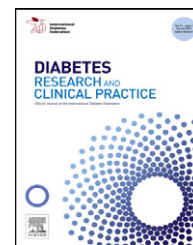
La pubblicazione è resa disponibile sotto le norme e i termini della licenza di deposito, secondo quanto stabilito dalla Policy per l'accesso aperto dell'Università degli Studi di Firenze (<https://www.sba.unifi.it/upload/policy-oa-2016-1.pdf>)

Publisher copyright claim:

(Article begins on next page)

Contents available at [Sciverse ScienceDirect](http://www.sciencedirect.com)

Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres
**International
Diabetes
Federation**


Brief report

Glycated hemoglobin in ST-elevation myocardial infarction without previously known diabetes: Its short and long term prognostic role

Chiara Lazzeri^{*}, Serafina Valente, Marco Chiostrì, Claudio Picariello, Paola Attanà, Gian Franco Gensini

Intensive Cardiac Coronary Unit, Heart and Vessel Department, Azienda Ospedaliero-Universitaria Careggi, Florence, Italy

ARTICLE INFO

Article history:

Received 12 May 2011

Received in revised form

22 September 2011

Accepted 26 September 2011

Published on line 5 November 2011

Keywords:

STEMI

Glycated hemoglobin

Non diabetic

Prognosis

ABSTRACT

In 518 consecutive STEMI non-diabetic patients, glycated hemoglobin > 6.5% was not associated with increased short and long term mortality, but was associated with higher admission glucose values, worse in-hospital glycemic control and a higher incidence of acute insulin resistance (HOMA index).

© 2011 Elsevier Ireland Ltd. All rights reserved.

1. Introduction

Data on the prognostic role of glycated hemoglobin (HbA1c) in patients with acute myocardial infarction are still controversial [1–9].

We assessed the prognostic role of HbA1c for short and long term mortality in 518 consecutive patients with ST elevation myocardial infarction (STEMI) and without previously known diabetes. All were treated with mechanical revascularization.

2. Methods

From 1st January 2008 to 30th June 2010, 518 non-diabetic STEMI patients (within 12 h from symptoms' onset) were

admitted to our Intensive Cardiac Care Unit (ICCU) [10–14]. Renal replacement therapy and mechanical ventilation were used, when needed [10–13]. After PCI, fasting glucose, insulin [12,13], C-peptide, HbA1c, troponin I, uric acid, C-reactive protein, alanine aminotransferase (ALT), aspartate amino transferase (AST) [15], gammaglutamyl transferase (GGT) [16], NT-pro Brain Natriuretic Peptide (NT-pro BNP) [13], total cholesterol, triglycerides, HDL, fibrinogen and creatinine were measured. Glomerular filtration rate ($1 \text{ ml/min/1.73 m}^2$) was calculated [17] as well as LDL (nv 60–190). Peak glucose, peak Tn I and nadir glomerular filtration rate were also measured. Insulin resistance was defined by the Homeostatic Model Assessment (HOMA). HOMA was calculated according to the following formula: $\{[\text{fasting insulin (microU/ml)}] \times [\text{fasting glucose (mmol/l)}]\} / 22.5$ [27]. Subjects whose values exceeded the sex-specific 75th

^{*} Corresponding author. Tel.: +39 55 7947518.

E-mail address: lazzeric@libero.it (C. Lazzeri).

0168-8227/\$ – see front matter © 2011 Elsevier Ireland Ltd. All rights reserved.

doi:[10.1016/j.diabres.2011.09.028](https://doi.org/10.1016/j.diabres.2011.09.028)

percentile (i.e. 1.80 for women and 2.12 for men) were considered to have insulin resistance (HOMA-IR) [11,12,18].

The study protocol was in accordance with the Declaration of Helsinki and approved by the local Ethics Committee. Informed consent was obtained in all patients before enrolment.

3. Statistical analysis

Data are reported as frequencies (percentages) and medians (95% Confidence Interval – CI) and analyzed by means of χ^2 (or Fisher's exact test, when predicted counts in almost one cell were less than 5) for categorical variables and Mann–Whitney U-test for continuous variables (which, at Kolmogorov–Smirnov normality test, were almost all non-normally distributed), respectively. In-ICCU mortality was assessed by logistic regression; a univariant analysis identified parameters that were significantly associated with outcome and these were used as candidate variables in a multivariant logistic regression model. Nagelkerke pseudo- R^2 and Hosmer–Lemeshow goodness-of-fit analyses are reported. Since the multivariable model was slightly overfitted, due to the low number of events, the data was further assessed by plotting a receiver operating characteristic (ROC) curve with each patient's estimated probability of death, in order to determine the discrimination achieved by the area under the curve (AUC). Long time survival was explored by means of Kaplan–Meier analysis with respect to HbA1c as a dichotomous variable (Log-rank test has been reported), as well as, after proportionality of risk assessment with Cox regression analysis, in both a univariant and multivariant manner. In this latter analysis, variables for inclusion were carefully chosen, given the number of events available, to ensure parsimony of the final model; non-significant variables were dropped by means of backward selection. Dichotomous HbA1c was forced into the analyses. A p value <0.05 was considered statistically significant (SPSS 13.0; SPSS Inc., Chicago, IL).

4. Results

Patients with HbA1c $\geq 6.5\%$ showed higher values of admission, peak and discharge glucose ($p < 0.001$, <0.001 and <0.001 , respectively) and a higher incidence of HOMA positivity ($p = 0.001$) as well as higher values of ESR ($p < 0.001$), fibrinogen ($p < 0.001$) and triglycerides ($p = 0.001$) and lower values of HDL ($p = 0.018$). There were no differences in short and long-term mortality rates or in the use of devices. Independent predictors for in-hospital mortality were (multi-

variate backward logistic regression analysis): admission glycemia (OR: 3.95, 95%CI: 1.92–8.12, $p < 0.001$), eGFR (1 ml/min/1.73 m² increase) (OR: 0.96, 95%CI: 0.93–0.98, $p = 0.002$), peak Tn I (10 ng/ml increase) (OR: 1.03, 95%CI: 1.01–1.06, $p = 0.088$). Hosmer and Lemeshow test $\chi^2 = 2.58$, $p = 0.589$; Nagelkerke $R^2 = 0.46$; area under the ROC curve 93% (95%CI: 88–99%, $p < 0.001$). HbA1c was not associated with in-hospital death (OR: 7.21, 95%CI: 0.75–69.69, $p = 0.088$). At follow-up (median of 39.7 months (22.2–57.1)), the Kaplan–Meier survival curve showed no significant differences between patients with HbA1c $<6.5\%$ and those with $\geq 6.5\%$. Table 1 shows the Cox regression analysis for long term mortality.

5. Discussion

In patients without a history of diabetes, only small studies on the prognostic role of HbA1c with different methods and results exist [6–9]. In 150 non-diabetic patients with MI, mortality rate and the risk of cardiogenic shock increased with HbA1c [6]. In a high-risk MI population [8] HbA1c was a risk marker of death at follow-up in patients without a history of diabetes and not in diabetic patients. In a small group of MI patients (diabetic and non-diabetic) treated with thrombolysis [7], there were significant relationships between admission glucose, HbA1c level and mortality at follow-up. Conversely, in 504 unselected, consecutive non-diabetic STEMI patients submitted to PCI, hyperglycemia (not glycated hemoglobin) was a predictor of 30-day outcome [9]. The main finding of our investigation is that HbA1c values were not related to mortality, short and long term, in consecutive STEMI patients without previously known diabetes, who were submitted to mechanical revascularization. In our investigation, patients with HbA1c levels higher than 6.5% did not show a higher infarct size (as indicated by Tn I and left ventricular ejection fraction) or a more critically illness (as inferred by the use of devices). Discrepancies with previous papers are mainly related to number consistency [6], population selection criteria [7] and type of revascularization [9]. Different from previous studies [6–9], we observed for the first time that higher HbA1c values helps in identifying a subset of patients who, in the early phase of STEMI, show an abnormal glucose response to stress as indicated by higher values of glucose, worse glycemic control during ICCU stay (peak glycemia) and a higher incidence of acute insulin resistance (HOMA index). All these factors have been associated with increased risk of early death by others [19] and us [10–12,18,20].

Patients with HbA1c $> 6.5\%$ also showed a increased inflammatory activation (increased values of fibrinogen and ESR), suggesting a link between acute glucose dysmetabolism and inflammation in the early phase of STEMI [19,20].

In conclusion, though increased values of HbA1c are not associated with a worse prognosis, non-diabetic STEMI patients with HbA1c $> 6.5\%$ may merit closer attention to in-hospital glucose management, since they exhibit an abnormal glucose response to stress.

Conflict of interest

The authors declare that they have no conflict of interest.

Table 1 – Adjusted Cox regression analysis.

	HR	95%CI	p	Wald
Age (1 year step)	1.054	1.018–1.092	0.003	8.828
Discharge LVEF (1% step)	0.951	0.914–0.990	0.014	6.028
Nadir eGFR (1 ml/min/1.73 m ² step)	0.981	0.963–0.999	0.045	4.023
HbA1c $>6.5\%$	0.705	0.213–2.338	0.568	0.326
LVEF: left ventricular ejection fraction; eGFR: estimated glomerular filtration rate.				

REFERENCES

- [1] Stolker JM, Sun D, Conaway DG, Jones PG, Masoudi FA, Peterson PN, et al. Importance of measuring glycosylated hemoglobin in patients with myocardial infarction and known diabetes mellitus. *Am J Cardiol* 2010;105(8):1090–4.
- [2] Malmberg K, Ryden L, Wedel H, et al. Intense metabolic control by means of insulin in patients with diabetes mellitus and acute myocardial infarction (DIGAMI 2): effects on mortality and morbidity. *Eur Heart J* 2005;26:650–61.
- [3] Malmberg K, Norhammar A, Wedel H, et al. Glycometabolic state at admission: important risk marker of mortality in conventionally treated patients with diabetes mellitus and acute myocardial infarction: long-term results from the Diabetes and Insulin-Glucose Infusion in Acute Myocardial Infarction (DIGAMI) study. *Circulation* 1999;99:2626–32.
- [4] Tenerz A, Nilsson G, Forberg R, et al. Basal glucometabolic status has an impact on longterm prognosis following an acute myocardial infarction in non-diabetic patients. *J Int Med* 2003;254:494–503.
- [5] Bartnik M, Malmberg K, Norhammar A, et al. Newly detected abnormal glucose tolerance: an important predictor of long-term outcome after myocardial infarction. *Eur Heart J* 2004;25:1990–7.
- [6] Oswald GA, Corcoran S, Yudkin JS. Prevalence and risks of hyperglycaemia and undiagnosed diabetes in patients with acute myocardial infarction. *Lancet* 1984;1:1264–7.
- [7] Rasoul S, Ottervanger JP, Bilo HJ, Timmer JR, van't Hof AW, Dambrink JH, et al. Glucose dysregulation in nondiabetic patients with ST-elevation myocardial infarction: acute and chronic glucose dysregulation in STEMI. *Neth J Med* 2007;65(Mar (3)):95–100.
- [8] Gustafsson I, Kistorp CN, James MK, Faber JO, Dickstein K, Hildebrandt PR. OPTIMAAL Study Group. Unrecognized glycometabolic disturbance as measured by hemoglobin A1c is associated with a poor outcome after acute myocardial infarction. *Am Heart J* 2007;154:47026.
- [9] Cakmak M, Cakmak N, Cetemen S, Tanriverdi H, Enc Y, Teskin O, et al. The value of admission glycosylated hemoglobin level in patients with acute myocardial infarction. *Can J Cardiol* 2008;24(5):375–8.
- [10] Lazzeri C, Chiostrì M, Sori A, Valente S, Gensini GF. Postprocedural hyperglycemia in ST elevation myocardial infarction submitted to percutaneous coronary intervention: a prognostic indicator and a marker of metabolic derangement. *J Cardiovasc Med (Hagerstown)* 2010;11(1):7–13.
- [11] Lazzeri C, Sori A, Chiostrì M, Picariello C, Gensini GF, Valente S. Prognostic role of insulin resistance as assessed by homeostatic model assessment index in the acute phase of myocardial infarction in nondiabetic patients submitted to percutaneous coronary intervention. *Eur J Anaesthesiol* 2009;26(10):856–62.
- [12] Lazzeri C, Valente S, Chiostrì M, Picariello C, Gian Franco Gensini. Correlates of acute insulin resistance in the early phase of non-diabetic ST-elevation myocardial infarction. *Diabetes Vasc Dis Res* 2011;8(1):35–44.
- [13] Valente S, Lazzeri C, Chiostrì M, et al. NT-proBNP on admission for early risk stratification in STEMI patients submitted to PCI Relation with extension of STEMI and inflammatory markers. *Int J Cardiol* 2009;132(1):84–9.
- [14] European Association for Percutaneous Cardiovascular Interventions, Wijns W, Kolh P, Danchin N, Di Mario C, Falk V, et al. Guidelines on myocardial revascularization: the task force on myocardial revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J* 2010;31(October (20)):2501–55.
- [15] Lazzeri C, Valente S, Tarquini R, Chiostrì M, Picariello C, Gensini GF. Prognostic values of admission transaminases in ST-elevation myocardial infarction submitted to primary angioplasty. *Med Sci Monit* 2010;16(November (12)):CR567–74.
- [16] Lazzeri C, Valente S, Tarquini R, Chiostrì M, Picariello C, Gensini GF. The prognostic role of gamma-glutamyltransferase activity in non-diabetic ST-elevation myocardial infarction. *Int Emerg Med* September:2010 [Epub ahead of print].
- [17] Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med* 2009;150(9):604–12.
- [18] Lazzeri C, Valente S, Chiostrì M, Picariello C, Gensini MDGF. Acute glucose dysmetabolism in the early phase of ST-elevation myocardial infarction: the age response. *Diabetes Vasc Dis Res* 2010;7(April (2)):131–7.
- [19] Deedwania P, Kosiborod M, Barrett E, et al. American Heart Association Diabetes Committee of the Council on Nutrition, Physical Activity and Metabolism. Hyperglycemia and acute coronary syndrome: a scientific statement from the American Heart Association Diabetes Committee of the Council on Nutrition, Physical Activity, and Metabolism. *Circulation* 2008;117(12):1610–9.
- [20] Lazzeri C, Valente S, Chiostrì M, Picariello C, Gensini GF. In-hospital peak glycemia and prognosis in STEMI patients without previously known diabetes. *Eur J Cardiac Prevent Rehabil* 2010;17(August (4)):419–23.